

CLAIMS

1. A pharmaceutical composition comprising balaglitazone and one or more other anti-diabetic compounds.

5 2. A composition according to claim 1 wherein said anti-diabetic compound is selected from amongst insulin together with derivative and analogues thereof, insulin secretagogues, insulin sensitizers, biguanides, α -glucosidase inhibitors, potassium channel openers, glucagon antagonists, protein tyrosine phosphatase inhibitors, glucokinase activators, RXR agonists, hormone sensitive lipase inhibitors, glycogen synthase kinase-3 inhibitors, glycogen phosphorylase inhibitors, glucose uptake modulators and lipid lowering compounds.

15 3. A composition according to claim 2, wherein said insulin, insulin analogue or insulin derivative is selected from amongst human insulin, human insulin wherein position B28 is Asp, Lys, Leu, Val or Ala and position B29 is Lys or Pro, B28Lys-B29Pro human insulin, des(B28-B30) human insulin, des(B27) human insulin, des(B30) human insulin, B29-N^e-myristoyl-des(B30) human insulin, B29-N^e-palmitoyl-des(B30) human insulin, B29-N^e-myristoyl human insulin, B29-N^e-palmitoyl human insulin, B28-N^e-myristoyl Lys^{B28} Pro^{B29} human insulin, B28-N^e-palmitoyl Lys^{B28} Pro^{B29} human insulin, B30-N^e-myristoyl-Thr^{B29} Lys^{B30} human insulin, B30-N^e-palmitoyl-Thr^{B29} Lys^{B30} human insulin, B29-N^e-(N-palmitoyl- γ -glutamyl)-des(B30) human insulin, B29-N^e-(N-lithocholyl- γ -glutamyl)-des(B30) human insulin, B29-N^e-(ω -carboxyheptadecanoyl)-des(B30) human insulin and B29-N^e-(ω -carboxyheptadecanoyl) human insulin.

25 4. A composition according to claim 2 wherein said insulin secretagogue is selected from amongst sulfonylureas, meglitinides and dipeptidyl peptidase inhibitors.

5. A composition according to claim 4, wherein said sulfonylurea is selected from amongst tolbutamide, glibenclamide, gliclazide, glimepiride, glipizid, chlorpropamide, tolazamide and glyburide.

30 6. A composition according to claim 4, wherein said meglitinides is selected from amongst nateglinide and repaglinide.

7. A composition according to claim 2, wherein said insulin sensitizer is selected from amongst troglitazone, ciglitazone, pioglitazone, rosiglitazone, isaglitazone, darglitazone, englitazone.

5 8. A composition according to claim 2, wherein said biguanide is metformin.

9. A compositions according to claim 2, wherein said α -glucosidase inhibitor is selected from amongst voglibose, emiglitate, miglitol and acarbose.

10 10. A composition according to claim 2, wherein said lipid lowering compound is a statin, fibrate or a PPAR δ agonist.

11. A composition according to claim 10, wherein said statin is selected form amongst atorvastatin, lovastatin, pravastatin, simvastatin, fluvastatin and cerivastatin.

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12. A composition according to claim 10, wherein said fibrate is selected from amongst fenofibrate, gemfibrozil, bezafibrate and PPAR α agonists.

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13. A composition according to any of claim 1-12, wherein balaglitazone and said other anti-diabetic compound are presented in two or more separate containers intended for sequentially or concomitantly use.

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14. A composition according to any of claims 1-12, wherein balaglitazone and said other anti-diabetic compound is presented in a single container.

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15. A method of treating conditions benefiting from a decrease in insulin resistance, a reduction of plasma glucose levels, a reduction of plasma fatty acid levels, a reduction of plasma triglyceride levels or a reduction of VLDL levels, the method comprising the administration of balaglitazone in combination with one or more other anti-diabetic compounds to a patient in need thereof.

16. The method according to claim 15, wherein said condition is selected from amongst type 2 diabetes, dyslipidemia, hyperglycemia, hyperinsulinemia, insulin resistance, obesity, cardiovascular complications, atherosclerosis, hypertension, impaired glucose tolerance, im-

paired fasting glucose level, increased plasma levels of free fatty acids, increased plasma levels of triglycerides, increased plasma levels of very low density lipoproteins (VLDL).

17. A method for increasing the plasma level of high density lipoproteins at the expense of the plasma level of VLDL, for decreasing the plasma glucose level, for decreasing the plasma level of free fatty acids, for decreasing the plasma triglyceride level, for delaying the progression of impaired glucose tolerance to non-insulin requiring type 2 diabetes, or for delaying the progression of non-insulin requiring type 2 diabetes to insulin requiring type 2 diabetes, the method comprising administering to a patient in need thereof an effective amount of balaglitazone in combination with one or more other antidiabetic compounds.

18. The method according to any of claims 15-17, wherein said other anti-diabetic agent is selected from amongst insulin together with derivative and analogues thereof, insulin secretagogues, insulin sensitizers, biguanides, α -glucosidase inhibitors, potassium channel openers, glucagon antagonists, protein tyrosine phosphatase inhibitors, glucokinase activators, RXR agonists, hormone sensitive lipase inhibitors, glycogen synthase kinase-3 inhibitors, glycogen phosphorylase inhibitors, glucose uptake modulators and lipid lowering compounds.

19. The method according to claim 18, wherein said insulin, insulin analogue or insulin derivative is selected from amongst human insulin, human insulin wherein position B28 is Asp, Lys, Leu, Val or Ala and position B29 is Lys or Pro, B28Lys-B29Pro human insulin, des(B28-B30) human insulin, des(B27) human insulin, des(B30) human insulin, B29-N^ε-myristoyl-des(B30) human insulin, B29-N^ε-palmitoyl-des(B30) human insulin, B29-N^ε-myristoyl human insulin, B29-N^ε-palmitoyl human insulin, B28-N^ε-myristoyl Lys^{B28} Pro^{B29} human insulin, B28-N^ε-palmitoyl Lys^{B28} Pro^{B29} human insulin, B30-N^ε-myristoyl-Thr^{B29} Lys^{B30} human insulin, B30-N^ε-palmitoyl-Thr^{B29} Lys^{B30} human insulin, B29-N^ε-(N-palmitoyl- γ -glutamyl)-des(B30) human insulin, B29-N^ε-(N-lithocholyl- γ -glutamyl)-des(B30) human insulin, B29-N^ε-(ω -carboxyheptadecanoyl)-des(B30) human insulin and B29-N^ε-(ω -carboxyheptadecanoyl) human insulin.

20. The method according to claim 18, wherein said insulin secretagogue is selected from amongst sulfonylureas, meglitinides and dipeptidyl peptidase inhibitors.

21. The method according to claim 20, wherein said sulfonylurea is selected from amongst tolbutamide, glibenclamide, gliclazide, glimepiride, glipizid, chlorpropamide, tolazamide and glyburide.

5 22. The method according to claim 20, wherein said meglitinides is selected from amongst nateglinide and repaglinide.

10 23. The method according to claim 18, wherein said insulin sensitizer is selected from amongst troglitazone, ciglitazone, pioglitazone, rosiglitazone, isaglitazone, darglitazone, englitazone.

24. The method according to claim 18, wherein said biguanide is metformin.

15 25. The method according to claim 18, wherein said α -glucosidase inhibitor is selected from amongst voglibose, emiglitate, miglitol and acarbose.

26. The method according to claim 18, wherein said lipid lowering compound is a statin, fibrate or PPAR δ agonist.

20 27. The method according to claim 26, wherein said statin is selected from amongst atorvastatin, lovastatin, pravastatin, simvastatin, fluvastatin and cerivastatin.

28. The method according to claim 26, wherein said fibrate is selected from amongst fenofibrate, gemfibrozil, bezafibrate and PPAR α agonists.

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29. The method according to any of claims 15-28, wherein the patient is obese.

30 30. The use of balaglitazone and one or more other anti-diabetic compound in the manufacture of a medicament for the treatment of type 2 diabetes, dyslipidemia, hyperglycemia, hyperinsulinemia, insulin resistance, obesity, cardiovascular complications, atherosclerosis, hypertension, impaired glucose tolerance, impaired fasting glucose level, increased plasma levels of free fatty acids, increased levels of plasma triglycerides, increased plasma levels of very low density lipoproteins (VLDL), or for the increase of the plasma level of high density lipoproteins at the expense of the plasma level of VLDL, for the decrease of the plasma glucose level, for the decrease of the plasma level of free fatty acids, for the decrease in the

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plasma level of triglycerides, for delaying the progression of impaired glucose tolerance to non-insulin requiring type 2 diabetes, or for delaying the progression of non-insulin requiring type 2 diabetes to insulin requiring type 2 diabetes, optionally in obese patients.

5 31. The use according to claim 30, wherein the medicament is intended for obese patients.

32. The use according to any of claims 30-31, wherein said anti-diabetic compound is selected from amongst insulin together with derivative and analogues thereof, insulin secretagogues, insulin sensitizers, biguanides, α -glucosidase inhibitors, potassium channel open-
 10 ers, glucagon antagonists, protein tyrosine phosphatase inhibitors, glucokinase activators, RXR agonists, hormone sensitive lipase inhibitors, glycogen synthase kinase-3 inhibitors, glycogen phosphorylase inhibitors, glucose uptake modulators and lipid lowering compounds.

15 33. The use according to claim 32, wherein said insulin, insulin analogue or insulin derivative is selected from amongst human insulin, human insulin where position B28 is Asp, Leu, Lys, Val or Ala and position B29 is Lys or Pro, B28Lys-B29Pro human insulin, des(B28-B30) human insulin, des(B27) human insulin, des(B30) human insulin, B29-N^E-myristoyl-des(B30) human insulin, B29-N^E-palmitoyl-des(B30) human insulin, B29-N^E-myristoyl human insulin,
 20 B29-N^E-palmitoyl human insulin, B28-N^E-myristoyl Lys^{B28} Pro^{B29} human insulin, B28-N^E-palmitoyl Lys^{B28} Pro^{B29} human insulin, B30-N^E-myristoyl-Thr^{B29}Lys^{B30} human insulin, B30-N^E-palmitoyl-Thr^{B29}Lys^{B30} human insulin, B29-N^E-(N-palmitoyl- γ -glutamyl)-des(B30) human insulin, B29-N^E-(N-lithocholyl- γ -glutamyl)-des(B30) human insulin, B29-N^E-(ω -carboxyheptadecanoyl)-des(B30) human insulin and B29-N^E-(ω -carboxyheptadecanoyl) human insulin.

25 34. The use according to claim 32, wherein said insulin secretagogue is selected from amongst sulfonylureas, meglitinides and dipeptidyl peptidase inhibitors.

30 35. The use according to claim 34, wherein said sulfonylurea is selected from amongst tolbutamide, glibenclamide, gliclazide, glimepiride, glipizid, chlorpropamide, tolazamide and glyburide.

36. The use according to claim 34, wherein said meglitinides is selected from amongst nateglinide and repaglinide.

37. The use according to claim 32, wherein said insulin sensitizer is selected from amongst troglitazone, ciglitazone, pioglitazone, rosiglitazone, isaglitazone, darglitazone, englitazone.

5 38. The use according to claim 32, wherein said biguanide is metformin.

39. The use according to claim 32, wherein said α -glucosidase inhibitor is selected from amongst voglibose, emiglitate, miglitol and acarbose.

10 40. The use according to claim 32, wherein said lipid lowering compound is a statin, fibrate or PPAR δ agonist.

41. The use according to claim 40, wherein said statin is selected from amongst atorvastatin, lovastatin, pravastatin, simvastatin, fluvastatin and cerivastatin.

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42. The use according to claim 40, wherein said fibrate is selected from amongst fenofibrate, gemfibrozil, bezafibrate and PPAR α agonists.

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